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Little is known about what constitutes appropriate care for older women with breast cancer. Extending work begun as part of an National Cancer Institute-funded project, we are examining whether variations in care received by older women affect short-term psychosocial and clinical outcomes. Our specific aims are: 1) To describe patterns of adjuvant hormonal and chemotherapy in older women, and factors associated with receipt of these therapies; 2) To characterize and quantify the breast cancer-related care received by older women during the early years following diagnosis; and 3) To determine the effects of ongoing breast cancer care on patients' quality of life.

We are conducting a longitudinal observational study of a cohort of 302 women ≥ 55 years of age diagnosed with stage I and II breast cancer between October 1992 and December 1995 at five sites in Boston, Massachusetts. Women are interviewed annually to obtain information about health and personal characteristics. Medical record abstracts are performed annually to gather information about treatments received, tests performed, and disease recurrences. Descriptive and multivariate analytic techniques will be used to identify patient and provider characteristics associated with variations in care received and the effects of these variations on patients' quality of life.

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Sherrie D. Kagle 8/29/96

PI - Signature Date

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5. INTRODUCTION

Nature of the Problem

Little is known about what constitutes appropriate care for older women with breast cancer (1) because until recently, women ≥ 70 years of age were excluded from most clinical trials. It is perhaps not surprising, therefore, that there is considerable variation in how older women are treated (2-9). There are several reasons why careful longitudinal observational studies involving older women with breast cancer need to be performed. First, because of spiraling health care costs, Congress and third party payers are demanding that we determine, insofar as possible, what constitutes effective care for our patients. Although randomized clinical trials will continue to be the gold standard for assessing treatment efficacy, large numbers of older women are not likely to be enrolled in such clinical trials and those that are enrolled will not be representative of those cared for by most practicing physicians (1). Second, the variations in diagnostic evaluation and initial treatment that have been observed may or may not matter in terms of important short and long-term clinical outcomes (recurrence and mortality) and in terms of psychosocial outcomes (physical, social, and emotional function). Evidence linking variations in care received by older patients and variations in clinical and psychosocial outcomes is sparse. For example, only very recently has the first study been published which links nondefinitive therapy with an increased risk of mortality (10). In addition there are limited data regarding psychosocial outcomes. However, there is evidence to suggest that more extensive surgery is a risk factor for poor upper body function among older women, but not for poor emotional function (11). Because of the chronic nature of early stage breast cancer, what happens in terms of follow-up care (adjuvant therapy and surveillance testing) may have a greater effect on patients' well-being than initial treatment. Third, because the incidence of breast cancer is continuing to rise, because the incidence increases with age (12), appearing only to level off at about age 80-85 (13), and because the numbers of women 65 years of age are rapidly increasing, the absolute number of new breast cancer cases will continue to grow into the foreseeable future, as will the proportion of cases involving older women.

Background/Previous Studies

The current study is designed to identify determinants of variations in adjuvant hormonal/chemotherapy and follow-up care among older women with early stage breast cancer and the effects of these variations on health-related quality of life and breast cancer-specific function.

Adjuvant Tamoxifen Therapy has both Benefits and Risks/Barriers

Benefits. Adjuvant tamoxifen therapy has been shown to decrease both rates of recurrence and mortality in older women with early stage breast cancer. A meta-analysis of clinical trials worldwide that included 2656 women ≥ 70 years of age, documented decreases in both recurrence (28%) and overall mortality (21%) rates among patients with node-positive disease treated with tamoxifen. Similar proportional risk reductions were found for node-negative patients, although the absolute risk reduction was greater for women who were node-positive. In

addition, the magnitude of risk reduction, both with respect to recurrence and mortality, was similar across three postmenopausal age groups: 50-59, 60-69, and 70+. Adjuvant tamoxifen therapy also was beneficial for women with hormone receptor-poor tumors, albeit to a lesser extent than in those with hormone receptor-rich tumors. Treatment with tamoxifen also prevents the development of contralateral breast cancer (14). There are non-breast cancer benefits of therapy for postmenopausal women as well. Tamoxifen may prevent osteoporosis (15) and lower cholesterol levels (16). Recent reports from Europe suggest that tamoxifen reduces the risk of hospitalization for cardiovascular disease and for fatal myocardial infarction (17-18).

Risks/Barriers to Treatment. Tamoxifen is prescribed as the result of a definite disease (breast cancer) in order to reduce the probability of events in the future: breast cancer recurrence; the development of contralateral breast cancer; death; and possibly, cardiovascular and osteoporotic complications. Although there are proven health benefits, the risks and costs are not insignificant. First, although some Medigap policies include a prescription medication benefit, many do not; most older persons must pay out-of-pocket for their medications, many of which cost a dollar or more per day (e.g., 19, 20). Generic tamoxifen, at the recommended dose of 20 mg/day, will cost most patients $85/month or more over a two to five year period. Second, taking tamoxifen may make patients feel worse, not better. One clinical trial involving younger postmenopausal women documented about a 4% dropout rate due to side effects, including nausea, hot flashes, edema, and vaginitis (21). Another clinical trial, also involving women < 65 years of age, documented persistent vasomotor, gynecological, or other major side effects in 48% of tamoxifen treated women compared with 21% of controls. Moderate to severe hot flashes, for example, persisted for 12 months in 22% of tamoxifen subjects vs. 5% of controls (22). In a clinical trial of women 65 - 84 years of age, Cummings and colleagues noted that 42% of women taking tamoxifen experienced mild toxicity symptoms by ECOG criteria, 21% experienced moderate symptoms, and 3% experienced severe symptoms (23). Third, treatment with tamoxifen increases the risk of rare, but serious illnesses. Deep vein thrombosis can complicate the use of tamoxifen and this risk appears to be greater in women ≥ 65 years (24). In addition, recent studies from Europe and the United States are relatively consistent in demonstrating an increased risk of endometrial cancer among tamoxifen users (25, 26). About 75% of endometrial cancers occur in women ≥ 60 years of age , and this already elevated base rate appears to be more than doubled by the addition of tamoxifen treatment (26). In light of the growing body of information about the risk of endometrial cancer, annual gynecological examinations, ranging from a history and physical examination to pelvic and/or endovaginal ultrasound and/or endometrial sampling are recommended for patients receiving tamoxifen (26). However, there is uncertainty as to the best approach to surveillance (27-29).

Evidence for Adjuvant Chemotherapy Treatment Efficacy

The value of adjuvant chemotherapy with or without tamoxifen in postmenopausal women is controversial, and in women over 70 years of age, has not been well-studied. In the meta-analysis described above, adjuvant chemotherapy resulted in only a 10% reduction in the mortality of women aged 60-69, although recurrences were reduced significantly. There were only 274 women enrolled in chemotherapy trials who were ≥ 70 years of age, and in these, adjuvant chemotherapy did not appear beneficial (14). Clearly adjuvant chemotherapy cannot be considered standard treatment for postmenopausal women, especially those ≥ 70 years of age. It

is possible, however, that adjuvant chemotherapy may be of benefit to subgroups of patients, especially those with aggressive disease. Because so little is known about the use of chemotherapy in older persons, the current project is addressing the following descriptive questions: 1) What proportion of older women, both with stage I and stage II breast cancer, currently receive adjuvant chemotherapy? and 2) What patient and physician characteristics are associated with the receipt of chemotherapy?

Surveillance for Recurrence following Initial Therapy

Although women are routinely followed by clinical examination and laboratory testing for evidence of recurrence, there is no evidence that this strategy results in earlier detection of recurrence or reduces mortality (30). Furthermore, case series evaluating the yield of various screening strategies have documented that most recurrences are detected either by patients themselves or by clinical examination (31-35). Only about 15% of recurrences are detected by surveillance testing which, in 1990 dollars amounts to an annual cost of about $1200/patient. No published studies have examined the costs and benefits, in human terms (either increasing anxiety or allaying fears), of surveillance testing, although a clinical trial evaluating these issues is reported to be in progress (35). Furthermore, none of the published studies have involved older women. Information about surveillance testing in older women is conspicuously lacking, including the types and frequency of testing and its impact on patient outcomes, particularly psychosocial outcomes. The current study is addressing the following questions: 1) How often are patients being seen and by which physicians during the early years following primary treatment? and 2) What are the types and frequency of surveillance tests and what are the effects of this testing on patient outcomes?

Summary: Given the national mandate to determine what constitutes effective health care and the fact that breast cancer is a disease primarily of older women (nearly half of newly diagnosed cases of breast cancer occur in women $\geq$ 65 years of age), we are conducting a longitudinal study of newly diagnosed older women with stage I and II disease: 1) to identify variations in follow-up care, and 2) to link these variations to patient outcomes. In conjunction with limited clinical trial data, this will be valuable information to assist clinicians in medical decision-making. Together, these two types of data will be able to inform the development of guidelines for the care of older women with breast cancer.

Purpose of the Current Study

As described above, we are filling important gaps in knowledge by addressing the following **study questions** in our current study:

1. What patient and provider characteristics are associated with the receipt of hormonal and/or chemotherapy?
2. What are the effects of hormonal treatment on patients' quality of life?
3. What patient and provider characteristics are associated with the receipt of surveillance tests?
4. What are the effects of surveillance testing on patients' quality of life?

Our specific aims are:

1. To describe patterns of adjuvant hormonal and chemotherapy in older women, and factors associated with receipt of these therapies.
2. To characterize and quantify the breast cancer-related care received by older women during the early years following diagnosis.
3. To determine the effects of ongoing breast cancer care (adjuvant therapy and disease surveillance) on patients' quality of life.

Overview of Methods of Approach

As described in more detail below (**6. BODY**), we are studying a cohort of women ≥ 55 years of age with newly diagnosed early stage breast cancer over a 2-5 year time period. Initial telephone interviews are conducted at 3-5 months following initial definitive treatment, with subsequent interviews occurring approximately two years later, and annually thereafter. Medical records are abstracted, beginning at the time of diagnosis and continuing until project completion, or the development of metastatic disease or subject death. The medical record review covering the initial treatment period and the baseline interview are funded by the National Cancer Institute. The follow-up interviews and medical record reviews are funded under the current project by the US Army Medical Research and Development Command.

6. BODY

Overview and Summary of Progress of Parent Study Funded by the National Cancer Institute (CA57754)

Funding from the National Cancer Institute (NCI) has enabled us to enroll the cohort that is being followed longitudinally for the current project. Patients ≥ 55 years of age with newly diagnosed early stage breast cancer, being cared for at one of five hospitals with academic affiliation in Boston, Massachusetts, were enrolled between January 1993 and April 1996. Eligible patients were sent an introductory letter signed by their surgeon and a consent form approximately three months following initial surgical treatment. This was followed by a telephone call from our interviewer who further explained the study, answered questions, and obtained informed consent. Data was collected via a review of patients' surgical records, and a 30 minute computer-assisted telephone interview with consenting eligible patients. Data collected from medical records included: histology, stage, estrogen receptor status, surgery performed, additional therapies received, and medical comorbidities.

Our patient telephone interview included questions about: general health-related quality of life, breast cancer-specific quality of life, medical comorbidities, the treatment decision-making process, treatment priorities, perceptions of doctor-patient communication, and demographic characteristics.

Results. Our overall response rate was 78%. Of 387 eligible patients, 302 participated. Non-participants were older (mean age=71.2 years for participants; 68.4 years for non-participants), but there was no difference in the proportion of participants and non-participants with stage I and stage II disease. Descriptive data on the 302 patients enrolled are presented in Tables 1-6. A

little over half of our subjects are ≥ 65 years of age and most are white. Half are married; most of the remainder are widowed. The majority have a high school education or greater. Our measure of comorbidity is a continuous measure based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease and related symptoms. In this sample the average score was 7.06 and ranged from 3.0 to 20. Positive scores reflect above average comorbidity. In addition, the majority of patients have infiltrating ductal carcinoma and have stage I disease. Of interest, stage I patients tend to be slightly older than stage II patients (68.9 vs. 66.6 years for mean age), perhaps reflecting the increasing use of mammography in older women. In dramatic contrast to patterns of care observed elsewhere among older women with breast cancer, the majority of our patients undergo breast conserving surgery. The majority also undergo an axillary dissection. While there is no relationship between age and type of surgery (mastectomy vs. breast conserving surgery) in our study sample, there is a relationship between age and whether women who undergo breast conserving surgery receive a course of radiation therapy (Table 4). Women ≥ 75 years of age who undergo breast conserving surgery are significantly less likely to receive a course of radiation therapy than are women < 75 years of age (p=0.006). Similarly, women ≥ 75 years of age are also significantly less likely to undergo axillary dissection (Table 5) than are their younger counterparts (p=0.000).

When asked about the helpfulness of breast cancer-related information received from a variety of sources, the information that was provided by their breast cancer physicians was rated as very or somewhat helpful by all responding patients. Written materials, both those provided by breast cancer physicians as well as those that patients obtained on their own, were also rated quite highly with respect to perceived helpfulness. Of less perceived helpfulness was information provided by friends and family, that from television specials, or that provided by the patient's family doctor, or the American Cancer Society.

We also asked patients about factors that were important in their decision-making. As can be seen, factors rated very important by almost all patients were two: 1) minimizing the possibility of recurrence, and 2) their doctors' recommendations. Although there was less consensus, also very important to the majority were quality of life after treatment and their family's opinion. In contrast, treatment-related factors were rated as not important at all by the majority of patients: 1) the effects of treatment on sexuality, 2) difficulty getting to and from treatments, and 3) the effects of treatment on looks. Half or close to half also stated that what they would have to pay out-of-pocket, the length of treatment, discomfort and disability following surgery, other side effects of treatment such as nausea and fatigue, and other post-surgical problems were not important at all in their decision-making process.

In summary, we have found that in the academic practices we are studying in Boston, the majority of older women with newly diagnosed early stage breast cancer receive breast conserving surgery, regardless of age. Nonetheless, there remain age-related variations in primary treatment: the receipt of axillary dissection overall, and the receipt of radiation therapy among those undergoing breast conserving surgery. These age-related variations in the care of the oldest old are comparable to those reported by us and others previously, and do not appear to be changing with time. This may well reflect continued uncertainty about the value of these interventions in women ≥ 75 years of age. In addition, our patients reported that minimizing the risk of recurrence and their doctors' recommendations were the two most important considerations in their treatment decision-making.

Experimental Methods Used for Current Study

Institutional Review Board Approval: All annual Institutional Review Board approvals have been obtained from each of the study sites. We received approval from Faulkner Hospital on November 14, 1995; from Boston Medical Center on November 15, 1995; from Boston City Hospital on December 27, 1995; from Beth Israel Hospital on October 16, 1995; and from New England Medical Center on December 12, 1995.

Study Implementation

Subject Enrollment and First Follow-up Interview in the Current Study. Subjects enrolled in the NCI study are mailed a consent packet 20 months after their diagnosis date. This time interval was chosen because it was the shortest interval from initial diagnosis possible with the initiation of the US Army Research and Development Command funding. To date, two hundred sixty-four patients from the cohort have been contacted to participate in the present study and 213 have completed their first follow-up interview. The non-participation rate is 14%. Fifteen patients could not be contacted because of changes in telephone numbers or addresses, or summer travel. An additional four patients had died and two were too ill to participate. Only 13 patients (5%) actually refused to participate. We will continue to enroll subject participants from the NCI project until all have reached 20 months of follow-up.

Second Follow-up Interview. Our second follow-up interview occurs approximately 12 months after the first follow-up interview. To date, 98 subjects have completed their second follow-up interview. A total of 17 (14%) have declined to participate. Seven could not be reached because residence and telephone numbers had changed. Five patients had died and two were too ill to participate. Only 3 (2%) refused to participate.

All women participating in the study as of July 1996 were sent a thank-you note, not only to express our appreciation for their involvement in the study thus far, but to maximize retention for the remainder of the project. A copy of the thank-you note is included in the Appendix.

Collection of Surveillance Data. Medical record abstractions were begun in November 1994, and a new medical record abstraction is performed annually for each participant. A data entry system was created with the same data quality checks as the interview data entry system. To assess inter-rater reliability, a 20% random sample of charts are reviewed by Dr. Silliman.

As each of our sites is a cancer center, we originally projected that we would be able to get a complete medical record abstraction, including adjuvant therapy and follow-up visit information from the records at each study site. Most of our study participants do receive their adjuvant treatment and follow-up care at the hospital where their surgery was performed. However, over the last year, thirty-two patients have had incomplete follow-up information in their study site medical record. We therefore developed a protocol to obtain the missing information from other doctor's offices and cancer care centers. The majority (59%) of the missing information were medical oncologists' notes, reports, and correspondence. Other missing information ranged from radiation oncologists' reports, to primary care physicians' reports and gynecologists' reports. Our method of obtaining missing information has been successful; approximately 80% of the medical offices contacted have sent us the requested information.

Preliminary Results for Current Study

First Follow-Up Interview. Our first follow-up interview which is completed approximately 20 months after the date of diagnosis, focuses on adjuvant therapy and follow-up care. Preliminary results reflect 213 women who have completed their first follow-up interviews. Although we have experienced a 14% loss to follow-up, our follow-up sample is very similar to the full baseline sample. For example, at the time of diagnosis, 41% of the full sample were less than 65 years of age; in the follow-up sample, 43% of the women were less than 65 years of age at the time of diagnosis. Similarly, at the time of diagnosis, 65% of the full sample had stage I disease; in the follow-up sample, 68% of the women had stage I disease at the time of diagnosis.

Adjuvant Therapy. Sixty-seven percent of patients (n=141) reported that their physicians had recommended adjuvant tamoxifen therapy and 94% (n=133) of these women reported that they had actually begun tamoxifen therapy. Of the 133 patients who had taken tamoxifen at any time, 75 (56%) reported that they were experiencing side effects. Table 7 shows the type of side effects experienced by the women. The most common side effect reported was hot flashes, which were experienced by 75% of the women. Vaginitis and depression were two other side effects reported by an important minority of patients. Nonetheless, at the time of the interview, 114 patients (86%) reported that they were still taking tamoxifen.

Bivariate analyses demonstrate that although there is no significant difference between the proportion of stage I and stage II patients taking tamoxifen at the time of the interview, a higher proportion of stage II patients, as expected, were taking it: 61% of stage I patients; 74% of stage II patients. Within stage, similar proportions of younger ($\leq$ 69 years of age) and older ($>$ 70 years of age) women were taking tamoxifen. Among stage I patients, approximately 60% of both age groups reported that they were taking tamoxifen; among stage II patients, 72% of the younger group and 80% of the older group reported that they were taking tamoxifen. A larger proportion of younger women (74%) than older women (44%) reported that they were experiencing side effects from tamoxifen treatment. In spite of the fact that younger women were more likely to experience side effects, a similar proportion of younger and older women (84%; 86%) reported that they were still taking tamoxifen.

Only 38 (18%) patients reported that adjuvant chemotherapy was recommended, and all but one of these patients received treatment. Most (34 of 37) patients who began chemotherapy reported that they experienced side effects. Tables 8 shows the type of sides effects experienced by these patients. The two most commonly reported side effects, each reported by over 90% of the women, were hair loss and fatigue; 85% of women reported that they were troubled by nausea. However, only four patients did not complete a complete course of therapy.

Follow-up Care. Our subjects reported that they saw their family physicians about two times in the past year (mean=2.3), on average. Among patients who reported at least one visit, the mean number was slightly higher (mean=2.6). The mean number of visits to their breast cancer surgeon was 1.9; among those reporting at least one visit, the mean was 2.3. For all patients the mean number of visits to their medical oncologist was 1.6, while for patients reporting at least one visit it was 2.5. Finally, for radiation oncologist visits, the mean number of visits were 1.1 and 2.2 respectively. Across the entire sample, women reported making, on average, 4.6 visits to breast cancer specialists during the previous year.

Approximately 50% of women reported that they felt calm before their breast cancer-related visits, while 30% reported that they did not. Similarly, 21% of women reported that they felt upset before their visit, while 69% stated that they did not. The vast majority of women reported that they felt good after a visit with their breast cancer specialist. Only 3% of women stated that they felt scared after a visit; 94% reported that they felt confident. Future analyses using medical record abstract data will allow us to determine whether it is abnormal test results, or referrals for further testing, that explain why a few patients feel upset after their visits and, conversely, whether the vast majority leave feeling better because they have been declared disease free.

Patients were also asked about how they were coping with feelings and concerns in their life that may be affected by their breast cancer. Most women, almost two years beyond their breast care diagnosis, reported that they feel they are doing well managing long-term life concerns. However, 17% of women reported that they were concerned about who would care for them if their condition deteriorated, and 16% reported that they were worried about recurrence. Nonetheless, only 101 women felt worried about their family's ability to manage if they became sicker. Analyses examining the relationship of factors such as stage and test results to patient concerns will help us to understand the context of these women's responses.

Second Follow-Up Interview. Our second follow-up interview occurs approximately 12 months after the first interview and includes much of the same information as the first follow-up interview. In addition, it asks more specific questions about adjuvant tamoxifen therapy and gynecological surveillance and evaluation. We added these latter questions because of the concern about endometrial cancer risk and the uncertainty regarding the value of screening in this setting. To date, 98 subjects have completed their second follow-up interview. Again, non-participants appear to be similar to those continuing to participate, having similar mean ages at diagnosis: 66.6 for respondents and 68.6 for non-respondents. Non-respondents have a higher representation of stage II patients, which reflects the higher death rate among stage II versus stage I patients.

Adjuvant tamoxifen therapy and gynecological care. Patients are asked about their tamoxifen use in the second follow-up interview. We found that 64% of patients (n=63) had been prescribed tamoxifen. Of those who were not currently taking tamoxifen (n=45, 46%), 12 (27%) reported that their doctor had recommended tamoxifen, and only 2 of these chose not to take it. Ten patients had discontinued tamoxifen; 7 of whom stopped because of side effects: hot flashes (n=3), depression (n=3), nausea (n=3) and vaginitis (n=2). Of the current tamoxifen users (n=53), 57% reported experiencing side effects. The most common side effects were hot flashes (63%), vaginitis (13%), and depression (13%). In addition, 16 patients complained of 14 other side effects that they attributed to tamoxifen.

Patients were also asked about gynecological care they received. We asked patients who had ever taken tamoxifen if they were referred to a gynecologist. Of the 54 who responded, 21% had been referred to a gynecologist once they started using tamoxifen. For patients who received gynecological care, 22% had had a vaginal ultrasound, and 14% had had an endometrial biopsy.

Emotional Adjustment. Patients were asked how they felt they were doing with worries and feelings surrounding their cancer. More than half of the patients (61%) felt they were doing excellent or very good with dealing with feelings of anger, fear and grief. Similarly, over half of the patients felt they were doing excellent or very good with their worries regarding their family's ability to manage if they got sicker, or worries about who would take care of them if they got

sicker (59% and 50% respectively). However, approximately 17% of patients did not feel they were doing well with worries about recurrence of cancer. Nonetheless, after asking patients to respond to certain statements about how they were feeling about their lives, 81% responded they "enjoyed life", 93% had "accepted their illness", and 75% were "content with their quality of life". Of note, 26% of patients were concerned about the risk of cancer in their family members.

Plans for the 03 Project Year.

The third follow-up interview has been developed and pre-tested. This will be the final follow-up interview for this project. The interview is a subset of questions from the second follow-up interview. Questions that no longer pertain to patients three years after their primary treatment have been dropped, and in addition we will be asking more in depth questions about long term side-effects from surgery and radiation therapy.

Medical record abstracting will continue throughout the 03 Year using the form as originally developed. Each subject will have a medical record abstract form related to each year of follow-up after the completion of her initial definitive treatment. Medical abstracting will end if patients develop metastatic disease or die. If patients develop in-breast recurrence or contralateral disease, abstracting will be suspended until the second episode of definitive treatment has been completed. For each subject, medical record abstracting will continue until the four year anniversary date of their initial treatment.

For patients who have died, we will obtain copies of death certificates from the Massachusetts Department of Health to determine the cause of death.

7. CONCLUSIONS

Because the current project is as yet not complete, it is premature to speculate about project implications. However, it is important to note that several products have emanated thus far from the combination of the parent study and the current study.

1) Dr. Silliman (Principal Investigator) and colleagues submitted a grant proposal to the National Cancer Institute June 1, 1995 entitled "Adjuvant Tamoxifen Therapy in Old Age: Determinants and Consequences" (R01 CA/AG 70818). It was funded and is due to begin in September 1996.

2) Dr. Silliman is co-investigator on a proposal submitted by Dr. Marianne Prout on July 17, 1996 to the US Army Medical Research and Development Command entitled "A pilot study of methods to assess whether breast cancer affects the functional status of older women who are long-term survivors".

3) Dr. Silliman was invited to write an editorial as a companion to an article on age-related treatment variations published in the Journal of the National Cancer Institute June 4, 1996. A copy is included in the Appendix.

4) Dr. Silliman has been invited to speak at the Cancer in the Elderly 1996 Conference (November 1996), at the lecture series sponsored by the Massachusetts Department of Health (January 1997), and at a special meeting of medical oncology educators in Puerto Rico (February 1997).

5) Dr. Silliman continues to serve as a member of the External Advisory Committee for the Jonnson Comprehensive Cancer Center's (UCLA) Cancer Prevention and Control in Older Women initiative.

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Table 1. Patient Demographics (n=302)	
Characteristic	**n (%)**
Age	
55-64	123 (41)
65-74	111 (37)
75+	65 (22)
Race	
White	280 (94)
African-American	13 (4)
Other minority	7 (2)
Marital Status	
Married	148 (49)
Widowed	98 (33)
Single	23 (8)
Divorced/Separated	30 (10)
Education	
< High school	51 (17)
High school graduate	107 (36)
> High school	141 (47)

Table 2. Patient Clinical Characteristics (n=302)	
Characteristic	**mean (range)**
Comorbidity (Casemix)	7.06 (3.0 - 20)
	n (%)
Breast Cancer	
Histology	
Infiltrating ductal	259 (86)
Infiltrating lobular	31 (10)
Other	12 (4)
Stage	
I	196 (65)
II	104 (35)

Table 3. Primary Tumor Management (n=302)	
	n (%)
Type of Surgery	
Breast conserving	227 (76)
Mastectomy	71 (24)
Axillary Dissection	
Yes	258 (86)
No	43 (14)

Table 4. Age and Radiation Therapy Following Breast Conserving Surgery (n=302)	
Age	**n (%)**
55-64	77 (90)
65-74	83 (91)
75+	33 (69)

Table 5. Age and Axillary Dissection (n=302)	
Age	**n (%)**
55-64	120 (98)
65-74	101 (91)
75+	34 (52)

Table 6. Patient Breast Cancer Treatment Decision-Making (n=302)	
	n (%)
Information sources perceived somewhat or very helpful in decision-making	
Breast cancer physicians or staff	294 (99)
Written materials from breast cancer physicians	248 (84)
Other written materials obtained by patient	198 (67)
Friends and family	161 (54)
Television	139 (47)
Family doctor	120 (41)
American Cancer Society	70 (24)
Factors very important in decision-making	
Minimizing recurrence	293 (99)
Doctors' recommendations	283 (96)
Quality of life after treatment	225 (77)
Family's opinion	153 (52)
Factors not important in decision-making	
Effects of treatment on sexuality	244 (83)
Difficulty getting to and from treatments	190 (65)
Effects of treatment on looks	185 (63)
What they would have to pay out-of-pocket	153 (52)
Length of treatment	135 (46)
Discomfort and disability following surgery	132 (45)
Other side effects of treatment	133 (45)
Other post-surgical problems	129 (44)

Table 7. Reported Side Effects of Tamoxifen Treatment (n=75)	
Type of Side Effect	**n (%)**
Hot flashes	56 (75)
Vaginitis	21 (28)
Depression	18 (24)
Nausea	8 (11)
Phlebitis	3 (4)
Edema	3 (4)
Other	30 (40)

Table 8. Reported Side Effects of Chemotherapy (n=34)	
Type of Side Effect	**n (%)**
Hair loss	31 (91)
Fatigue	32 (94)
Nausea	29 (85)
Depression	19 (56)
Flu Symptoms	16 (47)
Mouth Sores	12 (35)
Other	10 (29)

Appendix A

On behalf of our research team at the Boston University Medical Center I want to thank you for helping us with our breast cancer project. This project began in 1993, and to date over 300 of you have participated. Through telephone interviews you have provided information about treatment decision-making. In addition, many of you have completed subsequent interviews to discuss the follow-up care that you receive. Again, we would like to thank you for your help with our project, and hope you enjoy speaking with Elaine Abrams, our interviewer. Results of our project will be made available to you upon completion of our research. Please feel free to call or write us if you have questions or suggestions.

The Breast Cancer Study Team

Appendix B

Breast Cancer Care in Old Age: Where Do We Go From Here?

*Rebecca A. Silliman**

Breast cancer is a disease primarily of older women. The cumulative risk for this disease reaches its maximum well into the ninth decade of life (*1*). It is also a serious disease in older women. The approximate 10-year risk of disease recurrence for women 70 years of age or older who are lymph node negative with 1- to 5-cm tumors is 20%-30%; the risk for women with one to three positive lymph nodes and tumors of any size is 50%; the risk for women with four or more positive lymph nodes and tumors of any size is 80% (*2*). These risks are especially clinically relevant because recent gains in life expectancy have occurred at the end of life: The average life expectancy of an 85-year-old woman is nearly 6.5 years (*3*).

During the past decade, several studies (*4-9*) have documented age-related variations in care among patients with early stage breast cancer. These studies were conducted in a variety of health care settings and geographic regions. They have demonstrated age-related differences in diagnostic and prognostic evaluation as well as in initial treatment patterns. As a result of these studies, there has been heightened interest in understanding, in particular, variations in the use of mastectomy versus breast-conserving surgery with or without radiation therapy among older women and the impact of these variations on patient outcomes.

In this issue of the Journal, Ballard-Barbash et al. (*10*) have added to our understanding of age-related variations in breast cancer care through the use of a unique dataset that links Medicare[1] claims records with data from nine tumor registries participating in the Surveillance, Epidemiology, and End Results (SEER) Program.[2] Studying older women with newly diagnosed early stage disease, these investigators have documented the independent effects of age and comorbidity on the use of breast-conserving surgery versus mastectomy and on the use of radiation therapy following breast-conserving surgery. Specifically, they found that women aged 80 years or more, those with two or more comorbid conditions, and those with stage I disease were more likely to receive breast-conserving surgery. In contrast, among those receiving breast-conserving surgery, the oldest old (≥80 years of age) were much less likely to receive postoperative radiation therapy. In multivariate modeling, both age and comorbidity were independently associated with the receipt of postoperative radiation therapy. The oldest old and those with two or more comorbid conditions were less likely to receive radiation therapy.

Particular strengths of this study include the enrollment of a large cohort of patients (n = 18 704) cared for in nine different geographic settings, the careful attention to statistical control for potentially confounding factors, and the use of a validated measure of comorbidity. Nonetheless, the limitations of the data raise questions about the validity and the interpretation of the findings.

First, differential ascertainment of comorbidity may have importantly biased the data. A comorbidity score could not be calculated for 15% of the sample. Moreover, the authors note that only 36% of women who underwent breast-conserving surgery without axillary lymph node dissection had a reference hospitalization identified for the purpose of calculating the comorbidity index. Since it is the oldest old who are least likely to undergo axillary lymph node dissection (*8*), underascertainment of comorbidity in this group may have magnified the independent effect of age on the receipt of treatment. This possibility is supported by the fact that, for example, although there were 1352 women 80 years old or older who underwent breast-conserving surgery, only 220 of the entire sample undergoing breast-conserving surgery had two or more clinically important comorbid conditions. Not only do 80% of persons 65 years old or older have at least one chronic condition, but also the prevalence of chronic diseases increases dramatically with age, and multiple chronic conditions are especially common among older women (*11*).

Second, as Ballard-Barbash et al. (*10*) noted, the SEER database does not contain any information about functional status, social support, or patient preferences. In old age, functional status is a better predictor of mortality and other adverse events such as nursing home placement than is comorbidity (*12*). Furthermore, impaired function and diminished social support are particularly common among the oldest old. In particular, because of gender disparities in life expectancy, older women are frequently single and lack family or other supports (*13*). Because functional status and social support issues may limit an older woman's ability both to access and to tolerate radiation therapy, forgoing postoperative radiation therapy may not be an unreasonable decision, particularly in view of data not only suggesting low disease recurrence rates among older women receiving breast-conserving surgery but no postoperative radiation therapy (*14-16*), but also suggesting no significant survival advantage for those receiving breast-conserving surgery plus postoperative radiation therapy in comparison with those receiving breast-conserving surgery alone (*17*).

Third, the SEER database also does not contain any information about tamoxifen therapy. For example, we do not know how many women who underwent breast-conserving surgery

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See "Notes" section following "References."

were treated with tamoxifen in place of postoperative radiation therapy. Anecdotally, this pattern of care is relatively common among the oldest old, although this practice has not been studied systematically.

Fourth, and perhaps most importantly, the dataset does not include detailed outcome information. Indeed, few data are available that address outcomes among older women. What data there are suggest that, with respect to mortality, age-related variations in treatment patterns may be less important than stage (*1,18*). Furthermore, the oldest old are more likely to die with their disease rather than of it (*19,20*). Unfortunately, physicians are very inaccurate in their assessments of a given patient's future life expectancy, and we do not know how variations in treatment have an impact on the often more relevant outcomes of functional status and quality of life.

Given these limitations, where do we go from here? It is important to remember that age-related variations in care are not unique to breast cancer patients. Such variations have been noted not only in patients with other cancers (*21-23*), but also in patients with other diseases (*24,25*). The U.S. population is aging rapidly; yet we lack the scientific knowledge base to guide our clinical decision-making. Because of the increasing heterogeneity that is the hallmark of aging, generalizing from studies of younger patients is not always appropriate.

If we are to design studies to address questions of efficacy and effectiveness in old age, what are the essential elements that must be incorporated? First, we need studies of the oldest old. The findings reported by Ballard-Barbash et al. (*10*) highlight the fact that it is the group 80 years old or older about whom we know very little; this lack of knowledge is manifested by large variations in how they are treated. Although efforts should be made to design clinical trials for this age group, the known barriers to enrolling these patients into such trials (*26,27*) mean that considerable education of physicians, patients, and their families will be required before such trials will be feasible, purely from the standpoint of sample size. Even if adequate sample sizes can be achieved, there will always be concerns about generalizability, which will be magnified only in studies of the oldest old.

Second, we need to conduct studies that include the broadest range of older patients. Most likely, these studies will be observational. Although methodologically challenging, they offer the best prospect for answering many of the questions about which we care most. For example, we might learn about variations in outcomes among patients who have received breast-conserving surgery, with or without postoperative radiation therapy, by performing careful follow-up studies of patients treated in geographic regions with high and low rates of postoperative radiation therapy following breast-conserving surgery. These studies will require careful attention to such potential confounding variables as functional status and health-related quality of life. Moreover, they must recognize that patients themselves are the best sources of this information. Investigators conducting research on aging have developed psychometrically sound methods for measuring these variables in older persons (*28*). These measures, however, have been incorporated infrequently into studies of cancer patients. Thoughtful incorporation of these measures into future studies will require the close collaboration of geriatricians, oncology specialists, epidemiologists, and health services researchers, at the very least.

Age is the most important risk factor for the development of breast cancer and many other diseases. Our challenge is to develop a sound body of scientific knowledge upon which we can draw to make the best decisions for and with our older patients. They deserve no less.

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Notes

[1]*Editor's note:* Medicare is the federal health care insurance program for people aged 65 and over and for the disabled.

[2]*Editor's note:* SEER is a set of geographically defined, population-based central tumor registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Each registry annually submits its cases to the NCI on computer tape. These computer tapes are then edited by the NCI and made available for analysis.

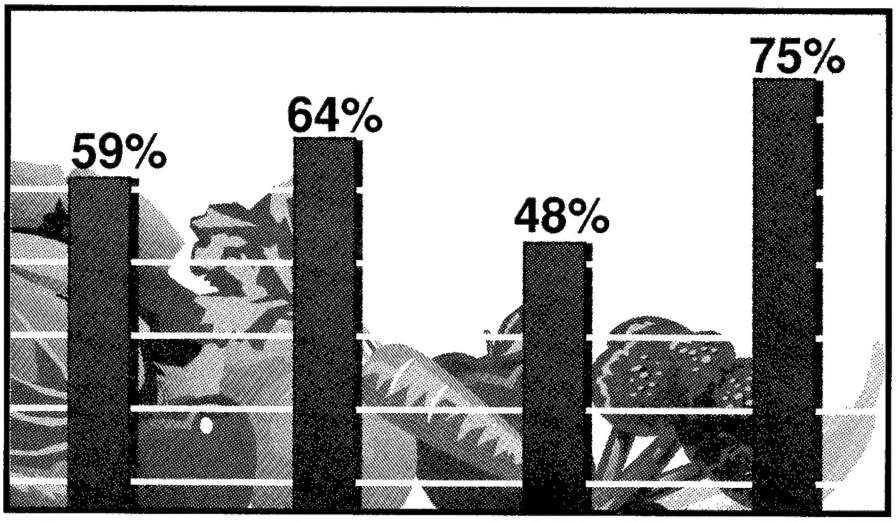
GETTING THE FACTS ON **5 A DAY**

How Americans are doing when it comes to fruits and vegetables

Why eat five?

As the link between diet and overall health continues to gain attention, public awareness of the benefits of fruits and vegetables has expanded. In a recent survey, 1,003 people were asked how likely they thought it is that eating fruits and vegetables can help reduce the risk of several health conditions.

Perceived health benefits most frequently mentioned were:



JOHN SHERLOCK

Source: National Cancer Institute

A National Cancer Institute Graphic